

REMARKS

The Examiner rejected claims 70-129, 131-133, 135-137, and 139-141. Claims 143-365 have been added herein. Thus, claims 70-129, 131-133, 135-137, 139-141, and 143-365 are pending. In addition, claims 127-129, 131-133, 135-137, and 139-141 have been amended to replace the term "comprises" with the term "is accompanied by." Applicant's specification as filed supports these claim amendments. Thus, no new matter has been added. In light of these amendments and the following remarks, Applicant respectfully requests reconsideration and allowance of claims 70-129, 131-133, 135-137, 139-141, 143-365.

Information Disclosure Statement

Applicant respectfully requests return of an initialed copy of the PTO-1449 form filed September 28, 2001. For the Examiner's convenience, a copy of the PTO-1449 form filed September 28, 2001 is attached hereto.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 127-129, 131-133, 135-137, and 139-141 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner stated that the phrase "non-invasive fungus-induced rhinosinusitis comprising the presence of allergic mucus" is vague and confusing. Likewise, the Examiner stated that the phrases "non-invasive fungus-induced rhinosinusitis comprising the presence of a polyp" and "non-invasive fungus-induced rhinosinusitis comprising the presence of eosinophilia" are vague and confusing. The Examiner asserted that it is unclear whether the presence of allergic mucus, a polyp, or eosinophilia are symptoms of the rhinosinusitis, or are contributed by the host. In addition, the Examiner suggested replacing the term "comprises" with the term "is accompanied by."

Applicant respectfully disagrees. A person having ordinary skill in the art would have understood the meaning of the phrases reciting that the non-invasive fungus-induced rhinosinusitis comprises the presence of allergic mucus, a polyp, or eosinophilia. To further

prosecution, however, the claims have been amended by replacing the term "comprises" with the term "is accompanied by" as suggested by the Examiner.

In light of the above, Applicant respectfully requests withdrawal of the rejection of claims 127-129, 131-133, 135-137, and 139-141 under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 70-129, 131-133, 135-137, and 139-141 under 35 U.S.C. §103(a) as being unpatentable over Cody *et al.* (In: *Rhinologic Diagnosis and Treatment*, Chapter 15, pp. 317-333 (1997)) in view of Bent *et al.* (*Allergy and Asthma Proc.*, 17:259-268 (1996)). Specifically, the Examiner stated that Cody *et al.* teach general methods for treatment of AFS, including nasal administration of antifungal agents or steroids. In addition, the Examiner stated that Bent *et al.* teach that AFS inherently includes the presence of polyps and allergic mucus, and the usefulness of topical steroids for AFS. The Examiner concluded that the subject matter defined by the claims would have been obvious within the meaning of 35 U.S.C. §103(a).

Applicant respectfully disagrees. The present claims recite methods for treating or preventing asthma and non-invasive fungus-induced rhinosinusitis. At no point do the Cody *et al.* or Bent *et al.* references, individually or collectively, disclose treating or preventing either asthma or non-invasive fungus-induced rhinosinusitis, let alone both asthma and non-invasive fungus-induced rhinosinusitis. In fact, neither the Cody *et al.* reference nor the Bent *et al.* reference discloses any treatment of asthma. Thus, the combination of cited references does not render the presently claimed invention obvious. In light of the above, Applicant respectfully requests withdrawal of the rejection of claims 70-129, 131-133, 135-137, and 139-141 under 35 U.S.C. §103(a).

CONCLUSION

Attached is a marked-up version of the changes being made by the current amendment. Applicant submits that claims 70-129, 131-133, 135-137, 139-141, and 143-365 are in condition for allowance, which action is requested. Filed herewith is a check in payment of the excess claim fees. The Examiner is invited to call the undersigned agent at the telephone number below


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Page : 28

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if such will advance prosecution of this application. Please apply any charges or credits to
Deposit Account No. 06-1050.

Respectfully submitted,

Date: October 10, 2001


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Version with markings to show changes made

In the claims

Claims 127-129, 131-133, 135-137, and 139-141 have been amended as follows:

127. The method of claim 70, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by the presence of a polyp.

128. The method of claim 70, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by the presence of allergic mucus.

129. The method of claim 70, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by eosinophilia.

131. The method of claim 121, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by the presence of a polyp.

132. The method of claim 121, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by the presence of allergic mucus.

133. The method of claim 121, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by eosinophilia.

135. The method of claim 122, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by the presence of a polyp.

136. The method of claim 122, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by the presence of allergic mucus.

137. The method of claim 122, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by eosinophilia.

139. The method of claim 124, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by the presence of a polyp.

140. The method of claim 124, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by the presence of allergic mucus.

141. The method of claim 124, wherein said non-invasive fungus-induced rhinosinusitis [comprises] is accompanied by eosinophilia.

Claims 143-365 have been added as follows:

143. The method of claim 70, wherein said mucoadministration begins during a period noncoincident with an intraoperative period, said intraoperative period being the time during a nasal surgery.

144. The method of claim 143, wherein said mammal had a nasal surgery before said mucoadministration.

145. The method of claim 143, wherein said mammal was nasal surgery-free before said mucoadministration.

146. The method of claim 121, wherein said mammal is a human.

147. The method of claim 121, wherein said mammal is nonatopic.

148. The method of claim 121, wherein said mammal is immunocompetent.

149. The method of claim 121, wherein said mucoadministration comprises direct mucoadministration.

150. The method of claim 121, wherein said method comprises mucoadministering said formulation to at least a portion of the nasal-paranasal anatomy of said mammal.

151. The method of claim 121, wherein said method comprises mucoadministering said formulation to at least a portion of the airways of said mammal.

152. The method of claim 121, wherein said method comprises mucoadministering said formulation to at least a portion of the lung airways of said mammal.

153. The method of claim 121, wherein said formulation is in a solid form.

154. The method of claim 121, wherein said formulation is in a liquid form.

155. The method of claim 121, wherein said formulation is in an aerosol form.

156. The method of claim 121, wherein said formulation is in a form selected from the group consisting of a powder, crystalline substance, gel, paste, ointment, salve, cream, solution, suspension, partial liquid, spray, nebulae, mist, atomized vapor, aerosol, and tincture.

157. The method of claim 121, wherein said mucoadministration comprises irrigating at least a portion of the nasal-paranasal anatomy of said mammal with a liquid form of said formulation.

158. The method of claim 121, wherein said mucoadministration comprises applying an aerosol form of said formulation to at least a portion of the nasal-paranasal anatomy of said mammal.

159. The method of claim 121, wherein said mucoadministration comprises applying a powder form of said formulation to at least a portion of the nasal-paranasal anatomy of said mammal.

160. The method of claim 121, wherein said antifungal agent comprises a macrolide.

161. The method of claim 121, wherein said antifungal agent comprises an azole.

162. The method of claim 121, wherein said antifungal agent interpolates fungal cell wall components.

163. The method of claim 121, wherein said antifungal agent comprises a sterol inhibitor.

164. The method of claim 121, wherein said antifungal agent comprises an antifungal agent selected from the group consisting of amphotericin B, ketoconazole, itraconazole, saperconazole, voriconazole, flucytosine, miconazole, fluconazole, griseofulvin, clotrimazole, econazole, terconazole, butoconazole, oxiconazole, sulconazole, ciclopirox olamine, haloprogin, tolnaftate, naftifine, terbinafine hydrochloride, morpholines, nystatin, natamycin, butenafine, undecylenic acid, Whitefield's ointment, propionic acid, and caprylic acid.

165. The method of claim 121, wherein said antifungal agent comprises an antifungal agent selected from the group consisting of amphotericin B, ketoconazole, itraconazole, saperconazole, and voriconazole.

166. The method of claim 121, wherein said antifungal agent comprises amphotericin B.

167. The method of claim 121, wherein said antifungal agent comprises itraconazole.

168. The method of claim 121, wherein said formulation comprises a pharmaceutically acceptable aqueous vehicle.

169. The method of claim 168, wherein said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent per liter.

170. The method of claim 168, wherein said effective amount comprises about 0.01 mL to about 1 L of said formulation per nostril of said mammal.

171. The method of claim 168, wherein said effective amount comprises about 5 mL to about 100 mL of said formulation per nostril of said mammal.

172. The method of claim 168, wherein said effective amount comprises about 20 mL of said formulation per nostril of said mammal.

173. The method of claim 168, wherein said formulation comprises about 1 ng to about 500 mg of said antifungal agent per liter.

174. The method of claim 168, wherein said formulation comprises about 100 mg of said antifungal agent per liter.

175. The method of claim 168, wherein said formulation comprises a plurality of antifungal agents.

176. The method of claim 121, wherein said effective amount of said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent per kg of body weight of said mammal.

177. The method of claim 121, wherein said effective amount of said formulation comprises about 1 ng to about 500 mg of said antifungal agent per kg of body weight of said mammal.

178. The method of claim 121, wherein said effective amount of said formulation remains constant during said effective duration.

179. The method of claim 121, wherein said effective frequency of said mucoadministration is from about four times a day to about once every other week.
180. The method of claim 121, wherein said effective frequency of said mucoadministration is from about twice a day to about once a week.
181. The method of claim 121, wherein said effective frequency of said mucoadministration is more frequent than once a day.
182. The method of claim 121, wherein said effective frequency of said mucoadministration is more frequent than once a week.
183. The method of claim 121, wherein said effective duration is greater than about 7 days.
184. The method of claim 121, wherein said effective duration is greater than about 14 days.
185. The method of claim 121, wherein said effective duration is greater than about 30 days.
186. The method of claim 121, wherein said effective duration is greater than about 60 days.
187. The method of claim 121, wherein said effective duration is greater than about 90 days.
188. The method of claim 121, wherein said formulation comprises a compound selected from the group consisting of pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.
189. The method of claim 121, wherein said method comprises administering to said mammal a second formulation.

190. The method of claim 189, wherein said second formulation comprises a compound selected from the group consisting of antifungal agents, pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.

191. The method of claim 121, wherein said mucoadministration begins during a period noncoincident with an intraoperative period, said intraoperative period being the time during a nasal surgery.

192. The method of claim 191, wherein said mammal had a nasal surgery before said mucoadministration.

193. The method of claim 191, wherein said mammal was nasal surgery-free before said mucoadministration.

194. The method of claim 122, wherein said mammal is a human.

195. The method of claim 122, wherein said mammal is nonatopic.

196. The method of claim 122, wherein said mammal is immunocompetent.

197. The method of claim 122, wherein said mucoadministration comprises direct mucoadministration.

198. The method of claim 122, wherein said method comprises mucoadministering said formulation to at least a portion of the nasal-paranasal anatomy of said mammal.

199. The method of claim 122, wherein said method comprises mucoadministering said formulation to at least a portion of the airways of said mammal.

200. The method of claim 122, wherein said method comprises mucoadministering said formulation to at least a portion of the lung airways of said mammal.
201. The method of claim 122, wherein said formulation is in a solid form.
202. The method of claim 122, wherein said formulation is in a liquid form.
203. The method of claim 122, wherein said formulation is in an aerosol form.
204. The method of claim 122, wherein said formulation is in a form selected from the group consisting of a powder, crystalline substance, gel, paste, ointment, salve, cream, solution, suspension, partial liquid, spray, nebulae, mist, atomized vapor, aerosol, and tincture.
205. The method of claim 122, wherein said mucoadministration comprises irrigating at least a portion of the nasal-paranasal anatomy of said mammal with a liquid form of said formulation.
206. The method of claim 122, wherein said mucoadministration comprises applying an aerosol form of said formulation to at least a portion of the nasal-paranasal anatomy of said mammal.
207. The method of claim 122, wherein said mucoadministration comprises applying a powder form of said formulation to at least a portion of the nasal-paranasal anatomy of said mammal.
208. The method of claim 122, wherein said antifungal agent comprises a macrolide.
209. The method of claim 122, wherein said antifungal agent comprises an azole.
210. The method of claim 122, wherein said antifungal agent interpolates fungal cell wall components.

220. The method of claim 216, wherein said effective amount comprises about 20 mL of said formulation per nostril of said mammal.
221. The method of claim 216, wherein said formulation comprises about 1 ng to about 500 mg of said antifungal agent per liter.
222. The method of claim 216, wherein said formulation comprises about 100 mg of said antifungal agent per liter.
223. The method of claim 216, wherein said formulation comprises a plurality of antifungal agents.
224. The method of claim 122, wherein said effective amount of said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent per kg of body weight of said mammal.
225. The method of claim 122, wherein said effective amount of said formulation comprises about 1 ng to about 500 mg of said antifungal agent per kg of body weight of said mammal.
226. The method of claim 122, wherein said effective amount of said formulation remains constant during said effective duration.
227. The method of claim 122, wherein said effective frequency of said mucoadministration is from about four times a day to about once every other week.
228. The method of claim 122, wherein said effective frequency of said mucoadministration is from about twice a day to about once a week.
229. The method of claim 122, wherein said effective frequency of said mucoadministration is more frequent than once a day.

230. The method of claim 122, wherein said effective frequency of said mucoadministration is more frequent than once a week.

231. The method of claim 122, wherein said effective duration is greater than about 7 days.

232. The method of claim 122, wherein said effective duration is greater than about 14 days.

233. The method of claim 122, wherein said effective duration is greater than about 30 days.

234. The method of claim 122, wherein said effective duration is greater than about 60 days.

235. The method of claim 122, wherein said effective duration is greater than about 90 days.

236. The method of claim 122, wherein said formulation comprises a compound selected from the group consisting of pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.

237. The method of claim 122, wherein said method comprises administering to said mammal a second formulation.

238. The method of claim 237, wherein said second formulation comprises a compound selected from the group consisting of antifungal agents, pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.

239. The method of claim 122, wherein said mucoadministration begins during a period noncoincident with an intraoperative period, said intraoperative period being the time during a nasal surgery.

240. The method of claim 239, wherein said mammal had a nasal surgery before said mucoadministration.

241. The method of claim 239, wherein said mammal was nasal surgery-free before said mucoadministration.

242. The method of claim 122, said method comprising, after said mucoadministration, prophylactically mucoadministering to said mammal a prophylactic formulation in an amount, at a frequency, and for a duration effective to prevent said asthma or said non-invasive fungus-induced rhinosinusitis, said prophylactic formulation comprising an antifungal agent.

243. The method of claim 242, wherein said prophylactic mucoadministration comprises direct mucoadministration.

244. The method of claim 124, wherein said mammal is a human.

245. The method of claim 124, wherein said mammal is nonatopic.

246. The method of claim 124, wherein said mammal is immunocompetent.

247. The method of claim 124, wherein said mucoadministration comprises direct mucoadministration.

248. The method of claim 124, wherein said method comprises mucoadministering said formulation to at least a portion of the nasal-paranasal anatomy of said mammal.

249. The method of claim 124, wherein said method comprises mucoadministering said formulation to at least a portion of the airways of said mammal.

250. The method of claim 124, wherein said method comprises mucoadministering said formulation to at least a portion of the lung airways of said mammal.

251. The method of claim 124, wherein said formulation is in a solid form.

252. The method of claim 124, wherein said formulation is in a liquid form.

253. The method of claim 124, wherein said formulation is in an aerosol form.

254. The method of claim 124, wherein said formulation is in a form selected from the group consisting of a powder, crystalline substance, gel, paste, ointment, salve, cream, solution, suspension, partial liquid, spray, nebulae, mist, atomized vapor, aerosol, and tincture.

255. The method of claim 124, wherein said mucoadministration comprises irrigating at least a portion of the nasal-paranasal anatomy of said mammal with a liquid form of said formulation.

256. The method of claim 124, wherein said mucoadministration comprises applying an aerosol form of said formulation to at least a portion of the nasal-paranasal anatomy of said mammal.

257. The method of claim 124, wherein said mucoadministration comprises applying a powder form of said formulation to at least a portion of the nasal-paranasal anatomy of said mammal.

258. The method of claim 124, wherein said antifungal agent comprises a macrolide.

259. The method of claim 124, wherein said antifungal agent comprises an azole.

260. The method of claim 124, wherein said antifungal agent interpolates fungal cell wall components.

261. The method of claim 124, wherein said antifungal agent comprises a sterol inhibitor.

262. The method of claim 124, wherein said antifungal agent comprises an antifungal agent selected from the group consisting of amphotericin B, ketoconazole, itraconazole, saperconazole, voriconazole, flucytosine, miconazole, fluconazole, griseofulvin, clotrimazole, econazole, terconazole, butoconazole, oxiconazole, sulconazole, ciclopirox olamine, haloprogin, tolnaftate, naftifine, terbinafine hydrochloride, morpholines, nystatin, natamycin, butenafine, undecylenic acid, Whitefield's ointment, propionic acid, and caprylic acid.

263. The method of claim 124, wherein said antifungal agent comprises an antifungal agent selected from the group consisting of amphotericin B, ketoconazole, itraconazole, saperconazole, and voriconazole.

264. The method of claim 124, wherein said antifungal agent comprises amphotericin B.

265. The method of claim 124, wherein said antifungal agent comprises itraconazole.

266. The method of claim 124, wherein said formulation comprises a pharmaceutically acceptable aqueous vehicle.

267. The method of claim 266, wherein said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent per liter.

268. The method of claim 266, wherein said effective amount comprises about 0.01 mL to about 1 L of said formulation per nostril of said mammal.

269. The method of claim 266, wherein said effective amount comprises about 5 mL to about 100 mL of said formulation per nostril of said mammal.

270. The method of claim 266, wherein said effective amount comprises about 20 mL of said formulation per nostril of said mammal.

271. The method of claim 266, wherein said formulation comprises about 1 ng to about 500 mg of said antifungal agent per liter.

272. The method of claim 266, wherein said formulation comprises about 100 mg of said antifungal agent per liter.

273. The method of claim 266, wherein said formulation comprises a plurality of antifungal agents.

274. The method of claim 124, wherein said effective amount of said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent per kg of body weight of said mammal.

275. The method of claim 124, wherein said effective amount of said formulation comprises about 1 ng to about 500 mg of said antifungal agent per kg of body weight of said mammal.

276. The method of claim 124, wherein said effective amount of said formulation remains constant during said effective duration.

277. The method of claim 124, wherein said effective frequency of said mucoadministration is from about four times a day to about once every other week.

278. The method of claim 124, wherein said effective frequency of said mucoadministration is from about twice a day to about once a week.

279. The method of claim 124, wherein said effective frequency of said mucoadministration is more frequent than once a day.

280. The method of claim 124, wherein said effective frequency of said mucoadministration is more frequent than once a week.

281. The method of claim 124, wherein said effective duration is greater than about 7 days.

282. The method of claim 124, wherein said effective duration is greater than about 14 days.

283. The method of claim 124, wherein said effective duration is greater than about 30 days.

284. The method of claim 124, wherein said effective duration is greater than about 60 days.

285. The method of claim 124, wherein said effective duration is greater than about 90 days.

286. The method of claim 124, wherein said formulation comprises a compound selected from the group consisting of pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.

287. The method of claim 124, wherein said method comprises administering to said mammal a second formulation.

288. The method of claim 287, wherein said second formulation comprises a compound selected from the group consisting of antifungal agents, pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.

289. The method of claim 124, wherein said mucoadministration begins during a period noncoincident with an intraoperative period, said intraoperative period being the time during a nasal surgery.

290. The method of claim 289, wherein said mammal had a nasal surgery before said mucoadministration.

291. The method of claim 289, wherein said mammal was nasal surgery-free before said mucoadministration.

292. The article of manufacture of claim 125, wherein said mammal is a human.

293. The article of manufacture of claim 125, wherein said mucoadministration comprises direct mucoadministration.

294. The article of manufacture of claim 125, wherein said label or package insert comprises an indication that said formulation can be mucoadministered to at least a portion of the nasal-paranasal anatomy of said mammal.

295. The article of manufacture of claim 125, wherein said label or package insert comprises an indication that said formulation can be mucoadministered to at least a portion of the airways of said mammal.

296. The article of manufacture of claim 125, wherein said label or package insert comprises an indication that said formulation can be mucoadministered to at least a portion of the lung airways of said mammal.

297. The article of manufacture of claim 125, wherein said formulation is in a solid form.

298. The article of manufacture of claim 125, wherein said formulation is in a liquid form.

299. The article of manufacture of claim 125, wherein said formulation is in an aerosol form.

300. The article of manufacture of claim 125, wherein said formulation is in a form selected from the group consisting of a powder, crystalline substance, gel, paste, ointment, salve, cream, solution, suspension, partial liquid, spray, nebulae, mist, atomized vapor, aerosol, and tincture.
301. The article of manufacture of claim 125, wherein said antifungal agent comprises a macrolide.
302. The article of manufacture of claim 125, wherein said antifungal agent comprises an azole.
303. The article of manufacture of claim 125, wherein said antifungal agent interpolates fungal cell wall components.
304. The article of manufacture of claim 125, wherein said antifungal agent comprises a sterol inhibitor.
305. The article of manufacture of claim 125, wherein said antifungal agent comprises an antifungal agent selected from the group consisting of amphotericin B, ketoconazole, itraconazole, saperconazole, voriconazole, flucytosine, miconazole, fluconazole, griseofulvin, clotrimazole, econazole, terconazole, butoconazole, oxiconazole, sulconazole, ciclopirox olamine, haloprogin, tolnaftate, naftifine, terbinafine hydrochloride, morpholines, nystatin, natamycin, butenafine, undecylenic acid, Whitefield's ointment, propionic acid, and caprylic acid.
306. The article of manufacture of claim 125, wherein said antifungal agent comprises an antifungal agent selected from the group consisting of amphotericin B, ketoconazole, itraconazole, saperconazole, and voriconazole.
307. The article of manufacture of claim 125, wherein said antifungal agent comprises amphotericin B.

308. The article of manufacture of claim 125, wherein said antifungal agent comprises itraconazole.

309. The article of manufacture of claim 125, wherein said formulation comprises a pharmaceutically acceptable aqueous vehicle.

310. The article of manufacture of claim 309, wherein said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent per liter.

311. The article of manufacture of claim 309, wherein said effective amount comprises about 0.01 mL to about 1 L of said formulation per nostril of said mammal.

312. The article of manufacture of claim 309, wherein said effective amount comprises about 5 mL to about 100 mL of said formulation per nostril of said mammal.

313. The article of manufacture of claim 309, wherein said effective amount comprises about 20 mL of said formulation per nostril of said mammal.

314. The article of manufacture of claim 309, wherein said formulation comprises about 1 ng to about 500 mg of said antifungal agent per liter.

315. The article of manufacture of claim 309, wherein said formulation comprises about 100 mg of said antifungal agent per liter.

316. The article of manufacture of claim 309, wherein said formulation comprises a plurality of antifungal agents.

317. The article of manufacture of claim 125, wherein said effective amount of said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent per kg of body weight of said mammal.

318. The article of manufacture of claim 125, wherein said effective amount of said formulation comprises about 1 ng to about 500 mg of said antifungal agent per kg of body weight of said mammal.

319. The article of manufacture of claim 125, wherein said effective frequency of said mucoadministration is from about four times a day to about once every other week.

320. The article of manufacture of claim 125, wherein said effective frequency of said mucoadministration is from about twice a day to about once a week.

321. The article of manufacture of claim 125, wherein said effective frequency of said mucoadministration is more frequent than once a day.

322. The article of manufacture of claim 125, wherein said effective frequency of said mucoadministration is more frequent than once a week.

323. The article of manufacture of claim 125, wherein said effective duration is greater than about 7 days.

324. The article of manufacture of claim 125, wherein said effective duration is greater than about 14 days.

325. The article of manufacture of claim 125, wherein said effective duration is greater than about 30 days.

326. The article of manufacture of claim 125, wherein said effective duration is greater than about 60 days.

327. The article of manufacture of claim 125, wherein said effective duration is greater than about 90 days.

328. The article of manufacture of claim 125, wherein said formulation comprises a compound selected from the group consisting of pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.

329. The article of manufacture of claim 126, wherein said mammal is a human.

330. The article of manufacture of claim 126, wherein said mucoadministration comprises direct mucoadministration.

331. The article of manufacture of claim 126, wherein said label or package insert comprises an indication that said formulation can be mucoadministered to at least a portion of the nasal-paranasal anatomy of said mammal.

332. The article of manufacture of claim 126, wherein said label or package insert comprises an indication that said formulation can be mucoadministered to at least a portion of the airways of said mammal.

333. The article of manufacture of claim 126, wherein said label or package insert comprises an indication that said formulation can be mucoadministered to at least a portion of the lung airways of said mammal.

334. The article of manufacture of claim 126, wherein said formulation is in a solid form.

335. The article of manufacture of claim 126, wherein said formulation is in a liquid form.

336. The article of manufacture of claim 126, wherein said formulation is in an aerosol form.

337. The article of manufacture of claim 126, wherein said formulation is in a form selected from the group consisting of a powder, crystalline substance, gel, paste, ointment, salve, cream, solution, suspension, partial liquid, spray, nebulae, mist, atomized vapor, aerosol, and tincture.

338. The article of manufacture of claim 126, wherein said antifungal agent comprises a macrolide.

339. The article of manufacture of claim 126, wherein said antifungal agent comprises an azole.

340. The article of manufacture of claim 126, wherein said antifungal agent interpolates fungal cell wall components.

341. The article of manufacture of claim 126, wherein said antifungal agent comprises a sterol inhibitor.

342. The article of manufacture of claim 126, wherein said antifungal agent comprises an antifungal agent selected from the group consisting of amphotericin B, ketoconazole, itraconazole, saperconazole, voriconazole, flucytosine, miconazole, fluconazole, griseofulvin, clotrimazole, econazole, terconazole, butoconazole, oxiconazole, sulconazole, ciclopirox olamine, haloprogin, tolnaftate, naftifine, terbinafine hydrochloride, morpholines, nystatin, natamycin, butenafine, undecylenic acid, Whitefield's ointment, propionic acid, and caprylic acid.

343. The article of manufacture of claim 126, wherein said antifungal agent comprises an antifungal agent selected from the group consisting of amphotericin B, ketoconazole, itraconazole, saperconazole, and voriconazole.

344. The article of manufacture of claim 126, wherein said antifungal agent comprises amphotericin B.

345. The article of manufacture of claim 126, wherein said antifungal agent comprises itraconazole.

346. The article of manufacture of claim 126, wherein said formulation comprises a pharmaceutically acceptable aqueous vehicle.

347. The article of manufacture of claim 346, wherein said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent per liter.

348. The article of manufacture of claim 346, wherein said effective amount comprises about 0.01 mL to about 1 L of said formulation per nostril of said mammal.

349. The article of manufacture of claim 346, wherein said effective amount comprises about 5 mL to about 100 mL of said formulation per nostril of said mammal.

350. The article of manufacture of claim 346, wherein said effective amount comprises about 20 mL of said formulation per nostril of said mammal.

351. The article of manufacture of claim 346, wherein said formulation comprises about 1 ng to about 500 mg of said antifungal agent per liter.

352. The article of manufacture of claim 346, wherein said formulation comprises about 100 mg of said antifungal agent per liter.

353. The article of manufacture of claim 346, wherein said formulation comprises a plurality of antifungal agents.

354. The article of manufacture of claim 126, wherein said effective amount of said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent per kg of body weight of said mammal.

355. The article of manufacture of claim 126, wherein said effective amount of said formulation comprises about 1 ng to about 500 mg of said antifungal agent per kg of body weight of said mammal.

356. The article of manufacture of claim 126, wherein said effective frequency of said mucoadministration is from about four times a day to about once every other week.

357. The article of manufacture of claim 126, wherein said effective frequency of said mucoadministration is from about twice a day to about once a week.

358. The article of manufacture of claim 126, wherein said effective frequency of said mucoadministration is more frequent than once a day.

359. The article of manufacture of claim 126, wherein said effective frequency of said mucoadministration is more frequent than once a week.

360. The article of manufacture of claim 126, wherein said effective duration is greater than about 7 days.

361. The article of manufacture of claim 126, wherein said effective duration is greater than about 14 days.

Applicant : Jens Ponikau
Serial No. : 09/500,115
Filed : February 8, 2000
Page : 53

Attorney's Docket No.: 07039-104002

362. The article of manufacture of claim 126, wherein said effective duration is greater than about 30 days.

363. The article of manufacture of claim 126, wherein said effective duration is greater than about 60 days.

364. The article of manufacture of claim 126, wherein said effective duration is greater than about 90 days.

365. The article of manufacture of claim 126, wherein said formulation comprises a compound selected from the group consisting of pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.